

Applicant: Norman Latov et al.
Serial No.: 10/088,775
Filed: March 20, 2002
Page 9

Remarks

Claims 1-4, 7-12, and 14-35 are pending and under examination in the subject application. Applicants have hereinabove amended claims 1, 2, 4, 7, 14, 15, and 17. Applicants maintain that the amendments to the claims raise no issue of new matter. Support for the amendments to claim 1 can be found in the specification as originally filed at, inter alia, page 12, lines 4-17; page 8, lines 2-3; and at page 31, lines 7-8. Support for the amendments to claim 2 can be found in the specification as originally filed at, inter alia, page 13, line 25 to page 14, line 18; and at page 31, lines 7-8. Support for the amendments to claim 4 can be found in the specification as originally filed at, inter alia, page 14, lines 23-27. Support for the amendments to claim 7 can be found in the specification as originally filed at, inter alia, page 5, line 31 to page 7, line 10; and page 8, lines 2-3. Support for the amendments to claims 14, 15, and 17 can be found in the specification as originally filed at, inter alia, page 18, lines 1-7. Accordingly, applicants respectfully request entry of this Amendment. After entry of this Amendment, claims 1-4, 7-12, and 14-35 will be pending and under examination.

Claims Rejected Under 35 U.S.C. §112 (First Paragraph)

In the October 19, 2004 Office Action, the Examiner stated that claims 1-4, 7-12, 14, 15, and 17-35 are rejected under 35 U.S.C. §112, first paragraph, for both written description and enablement.

In response, applicants respectfully traverse the Examiner's rejection. Applicants note that the recited calcium salt forms of gangliosides were chosen for coating solid particles because free acid gangliosides were found to clump. In addition, the materials

Applicant: Norman Latov et al.
Serial No.: 10/088,775
Filed: March 20, 2002
Page 10

and methods section on page 31 of the specification clearly describes that *calcium salt forms* of the gangliosides were used. As such, applicants maintain that the calcium salt recitation in the claims is an actual exemplified embodiment, and that it is not new matter. Moreover, applicants maintain that the recited characteristic is explicitly described and clearly enabled in the specification as filed. Accordingly, respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Claims Rejected Under 35 U.S.C. §103(a)

The Examiner stated that claims 1-3, 10, 13, 14, and 17-19 are rejected under 35 U.S.C. §103(a) as being unpatentable over Uhlig et al. (Autoimmunity 5:87-89, 1989) in view of Dwyer et al., Uemura et al., Ravindranaths et al., Pestronk et al., and in Beltz et al. as previously cited.

In response, applicants respectfully traverse the Examiner's rejection. Specifically, applicants note that "Ca⁺⁺ salts" of gangliosides as recited in the claimed invention and employed by the applicants, are not explicitly taught by Uhlig et al. Furthermore, the assumption that the Type II ganglioside used by Uhlig et al. is a calcium salt is not supported in light of the fact that commercially available free acid gangliosides are also available (e.g. see Sigma catalogue page 918; **Exhibit A**, annexed hereto), especially in the absence of any mention by Uhlig et al. of ganglioside salt or Ca⁺⁺ salt.

Furthermore, Uhlig et al. in combination with the other cited references do not teach passive adsorption of a Ca⁺⁺ salt of the ganglioside to at least two separate solid particles, as recited in the claims. At most, Uhlig et al. discuss a liposome made from lipids including gangliosides (see page 94-95 of Uhlig et al. and

Applicant: Norman Latov et al.
Serial No.: 10/088,775
Filed: March 20, 2002
Page 11

page 91, "liposome preparation"), i.e. the ganglioside is a constituent of the liposome itself. The ganglioside is not a calcium salt form passively adsorbed onto the solid particle. The remaining cited references, in combination with Uhlig et al., do not cure this deficiency.

Moreover, Uhlig et al. in combination with the other cited references do not teach or suggest "contacting a liquid sample from the subject with the GM1, GM2, GM3, GD1, GD2, GD3, GD1a, GD1b, GT1b or GQ1b ganglioside, the ganglioside being affixed by passive adsorption of a Ca^{++} salt of the ganglioside to at least two separate solid particles" as recited in the claims.

In addition, in regard to claim 2, Uhlig et al. in combination with the other cited references do not teach or suggest a method comprising exposing a liquid sample to two different gangliosides, each affixed by passive adsorption of a Ca^{++} salt to at least two separate solid particles.

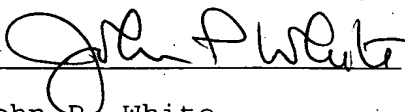
Accordingly, applicants maintain that the rejected claims define an invention not obvious from the cited references, and therefore respectfully request that the Examiner reconsider and withdraw this ground of rejection.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

Applicant: Norman Latov et al.
Serial No.: 10/088,775
Filed: March 20, 2002
Page 12

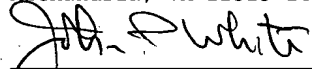
No fee, apart from the enclosed \$60.00 fee for a one month extension of time, is deemed necessary in connection with the filing of this Amendment. If any such fee is required, however, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



John P. White
Registration No. 28,678
Attorney for Applicants
Cooper & Dunham LLP
1185 Avenue of the Americas
New York, New York 10036
(212) 278-0400

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

 2/14/05
John P. White Date
Registration No. 28,678

2002-2003

cell
signaling

molecular
biology

**Biochemicals
and
Reagents
for Life Science
Research**

cell culture

reagents

OVER 5,000
NEW PRODUCTS

THE STANDARD
FOR SERVICE

RELIABLE PRODUCT
QUALITY

R & D
INNOVATION

WORLD'S LARGEST
SELECTION

protein
analysis

diagnostics

proteomics

equipment



SIGMA®

sigma-aldrich.com

AWARD-WINNING
WEB SITE

Applicant: Norman Latov et al.
U.S. Serial No.: 10/088,775
Filed: September 16, 2002
Exhibit A

US \$

(Continuation of)
Ganciclovir

- homologous recombination of a gene of interest is required.
- Color white
- $E_{254}^{1\% 1\text{cm}}$ 12.0
- Solubility
- 0.1 N HCl 10 mg/mL
- Ref.: 1. Sprung, C.N., et al., Chromosome healing in mouse embryonic stem cells. *Proc. Natl. Acad. Sci. USA* 96, 6781-6786 (1999)
2. Halloran, P.J., and Fenton, R.G., Irreversible G2-M arrest and cytoskeletal reorganization induced by cytotoxic nucleoside analogues. *Cancer Res.* 58, 3855-3865 (1998)
3. Rubsam, L.Z., et al., Cytotoxicity and accumulation of ganciclovir triphosphate in bystander cells cocultured with herpes simplex virus type 1 thymidine kinase-expressing human glioblastoma cells. *Cancer Res.* 59, 675 (1999)
4. Oon, C.J., et al., Hepatitis B virus variants with lamivudine-related mutations in the DNA polymerase and the 'a' epitope of the surface antigen are sensitive to ganciclovir. *Antiviral Res.* 41, 113-118 (1999)
5. Cannon, J.S., et al., Human herpesvirus 8-encoded thymidine kinase and phosphotransferase homologues confer sensitivity to ganciclovir. *J. Virol.* 73, 4786-4793 (1999)
6. Yamasaki, H., et al., Role of connexin (gap junction) genes in cell growth control and carcinogenesis. *C.R. Acad. Sci.* 322, 151-159 (1999)
- R: 46-60-61 S: 53-45-36/37/39

Ganglioside G_{D1b} , disialo See: Disialoganglioside G_{D1b} Page 725Ganglioside G_{D1b} , disialo See: Disialoganglioside- G_{D1b} Page 725Ganglioside G_{M1} , asialo See: Asialoganglioside G_{M1} Page 223Ganglioside G_{M2} , monosialo See: Monosialoganglioside G_{M2} Page 1437

G 2375 Gangliosides Purified 10 mg 59.20

from bovine brain 25 mg 108.90

Type III 100 mg 321.90

Gangliosides are major constituents of neuronal cell membranes and endoplasmic reticulum; contain a sialated polysaccharide chain linked to ceramide through a β -glycosidic linkage; for classification of gangliosides see Svennerholm, L., et al. (eds.), *Structure and Function of Gangliosides*, New York, Plenum, 1980.

A family of glycosphingolipids isolated from bovine brain

N-acetylneuraminic acid approx. 20%

Ref.: 1. Itoh, et al., Prevention of the death of the rat axotomized hypoglossal nerve and promotion of its regeneration by bovine brain gangliosides. *Glycobiology* 9, 1247-1252 (1999)

2. Yamakawa, Reflections on biochemistry. Thus started ganglioside research *Trends Biol. Sci.* 13, 452-454 (1988)

Ganglioside G_{T1b} See: Trisialoganglioside- G_{T1b} Page 2089Ganglioside G_{M1} , asialo See: Asialoganglioside G_{M1} Page 223Ganglioside G_{M2} , monosialo See: Monosialoganglioside G_{M2} Page 1437**G 6666** Monoclonal Anti-GAP1^{TP48P} 0.2 mL 194.95

from mouse

approx. 2 mg/mL, Buffered aqueous solution, Purified immunoglobulin, Clone GP-3

Immunogen: recombinant human GAP1^{TP48P}

Solution in 0.01 M phosphate buffered saline, pH 7.4, containing 15 mM sodium azide

Antigen mol wt approx. 100 kDa

Species reactivity: human

Application(s)

Immunocytochemistry suitable

Indirect ELISA suitable

Isotype IgG2b

Application(s)

Immunoblotting 1-2 μ g/mL using human platelets extract

GAP-DH See: Glyceraldehyde-3-phosphate Dehydrogenase Page 1430

Gardnerella vaginalis selective supplement 1 vial 28.00

G 4539 Composition: (per vial)

Gentamicin sulfate: 2.00 mg

Nalidixic acid: 15.00 mg

Amphotericin B: 1.00 mg

An antibiotic supplement recommended for the selective isolation of *Gardnerella vaginalis*.

Sufficient for 500 mL medium

R: 61-20/21-36/38-42/43 S: 53-22-45-36/37/39

Gassner lactose agar 500 g 66.40

G 9431 Ingredients (g/L)

Meat peptone, 7.00

Sodium chloride, 5.00

Lactose, 50.00

Metachrome yellow, 1.25

Water blue, 0.625

Agar, 13.00

Used for detection and isolation of pathogenic *Enterobacteriaceae*.

Ref.: Gassner, G., *Centralbl. Bakt. I. Orig.* 80, 219 (1918)

Gastric Inhibitory Polypeptide Human See: Gastrointestinal Peptides Page 921

Gastric Inhibitory Polypeptide Porcine See: Gastrointestinal Peptides Page 921

Monoclonal Anti-Gastric Mucin 0.2 mL 67.90

M 5293 from mouse 0.5 mL 133.90

Liquid, Ascites fluid, Clone 45M1

Immunogen: mucin from human ovarian cyst fluid

The product recognizes the mucin epitope g located in the peptide core of gastric mucin (>1,000 kDa). This epitope is completely destroyed by thiol reduction (using mercaptoethanol) and partially lost following trypsin proteolysis, but is stable upon periodate oxidation. The antibody reacts with ethanol-fixed, cultured epithelial cells and ethanol-fixed, formalin-fixed, paraffin-embedded tissue sections. It stains the surface gastric epithelium of normal human gastrointestinal tract and reacts with fetal, pre-cancerous and cancerous colonic mucosa, but not with normal colon. It may be used in immunoblotting (non-reducing conditions), immunocytochemistry, immunohistochemistry and immunoradiofixation. Enzymatic pretreatment of formalin-fixed, paraffin-embedded sections may enhance staining intensity.

Species reactivity: chicken, hedgehog, pig, rabbit, rat, mouse, monkey, human

contains 15 mM sodium azide

Application(s)

Immunoblotting suitable using non-reducing conditions

Immunohistochemistry (formalin-fixed, paraffin-embedded sections) 1:200 using formalin-fixed, paraffin-embedded sections of human stomach

Immunocytochemistry suitable

Isotype IgG1

Ref.: 1. Bara, J., et al., *J. Immunol. Meth.* 149, 105 (1992)

2. Bara, J., et al., *Int. J. Cancer* 47, 304 (1991)

Anti-Gastrin

0785 from rabbit

Liquid, W1

Immunogen: gastrin (1-13)

The antiserum against gastrin I by immunoprecipitation from duodenum

Species reactivity: contains 15 mM sodium azide

Application(s)

Radioimmunoassay

Sections of h

Gastrointestinal

These peptides, found in the body. They are involved in the regulation of the digestive system.

Alytesin

2803 pGlu-Gly-Ala-Val-Gly-Thr⁶-Bomk

[31078-12-minimum

Bombesin

the European

gical activity

Ref.: Anastasi

Arg-Arg-Gas

4535 Human

Arg-Arg-Leu

Ala-Tyr-Gly

[84424-84-

Substrate f

Ref.: Baldwin

656 (1982)

Big Gastrin I

HG-34; Hu

Gly-Pro-Prc

Gly-Pro-Trp

Trp-Met-As

[60675-77-

Storage for

activity.

Ref.: 1. Huss

vesicular mor

cells. *J. Physiol.*

2. Sawada, H.

expression (P

processing. *A*

minimum

Similar to (

Sigma.

Ref.: Bishop,

gastrin precu

terology 115

7264

minimum

Ref.: Bishop,

cleavage of t

prohormone

(1998)

**This Page is Inserted by IFW Indexing and Scanning
Operations and is not part of the Official Record**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ **BLACK BORDERS**
- ☐ **IMAGE CUT OFF AT TOP, BOTTOM OR SIDES**
- ☐ **FADED TEXT OR DRAWING**
- ☐ **BLURRED OR ILLEGIBLE TEXT OR DRAWING**
- ☐ **SKEWED/SLANTED IMAGES**
- ☐ **COLOR OR BLACK AND WHITE PHOTOGRAPHS**
- ☐ **GRAY SCALE DOCUMENTS**
- ☐ **LINES OR MARKS ON ORIGINAL DOCUMENT**
- ☐ **REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY**
- ☐ **OTHER:** _____

IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.